Attorney Docket No.: 14875-0154US1
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Applicant : Taro Miyazaki et al.
Serial No. : 10/560,098
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Art Unit : 1643
Examiner : Lynn Anne Bristol

Title : Process for Producing Antibodies

Examiner Lynn A. Bristol
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Examiner Bristol:

Attached is a draft amendment for discussion in our interview with you and SPE Blanchard on June 2, 2009 at 2:00 P.M. EDT. We suggest that since Dr. Frazer and I are in offices in different cities, the logistics of the call might be simpler if you called us on our toll-free dial in number. The number is 866-209-6438, participant code 466108. I will call you today to confirm.

Very truly yours,
Gretchen L. Temeles, Ph.D.
Reg. No. 57,077

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Examiner L. Bristol
USSN 10/560,098
Taro Miyazaki et al.

Attorney docket no. 14875-0154US1

DRAFT AMENDMENT
FOR DISCUSSION IN JUNE 2, 2009, TELEPHONIC INTERVIEW

For simplicity, this draft amendment omits the pending withdrawn claims.

1. (Currently amended) A method for producing an antibody wherein the method comprises expressing in a eukaryotic cell a first light chain and a first heavy chain beginning at one time and expressing in the same cell a second light chain and a second heavy chain beginning at a second, different time, wherein the amino acid sequences of the first heavy chain and second heavy chain are different and the amino acid sequences of the first light chain and the second light chain are different.

2. (Canceled)

3.-4. (Withdrawn)

5. (Canceled)

6. (Currently amended) The method of claim 1[[;]], wherein the antibody is a bispecific antibody, wherein the first light chain and the first heavy chain together recognize a first antigen and the second light chain and the second heavy chain together recognize a second antigen.

7. (Canceled)

8. (Previously presented) The method of claim 1, wherein the antibody is prepared using the knobs-into-holes technique

22. (Currently amended) The method of claim 1, wherein expression of the first light chain and the first heavy chain are under the control of a first expression regulator and the expression of the second light chain and the second heavy chain are under the control of a second expression regulator and the first and the second expression regulators are different ~~and wherein either: (i) the first light and heavy chains and he second light and heavy chains are all encoded by the same vector or (ii) the first light and heavy chains are encoded by a first vector and the second light and heavy chains are all encoded by a second, different vector~~.

23. (New) The method of claim 1, wherein the amino acid sequences of the first and second heavy chains comprise one or more mutations that promote the formation of hetero-multimers.

24. (New) The method of claim 1, wherein the heavy and first heavy and light chains are expressed for a period of time that does not overlap with the period of time when the second heavy and light chains are expressed.

25. (New) The method of claim 22, wherein each of the first light chain, the first heavy chain, the second light chain and the second heavy chain is encoded on a separate vector.

26. (New) The method of claim 22, where in the first light and heavy chains are encoded on a first vector and the second light and heavy chains are encoded on a second, different vector.

27. (New) The method of claim 22 wherein the first light chain, the first heavy chain, the second light chain and the second heavy chain are all encoded on a single vector.

28. (New) The method of claim 22, wherein one of the expression regulators is a tetracycline or an ecdysone analogue.

29. (New) A method for producing an antibody, the method comprising:

(a) providing a eukaryotic host cell containing (i) nucleic acid encoding a first light chain and a first heavy chain that bind to a first antigen, and (ii) nucleic acid encoding a second light chain and a second heavy chain that bind to a second antigen, wherein the amino acid sequences of the first heavy chain and second heavy chain are different and the amino acid sequences of the first light chain and the second light chain are different, and wherein the amino acid sequence of the first heavy chain comprises one or more mutations that promote the formation of hetero-dimers;

(b) causing expression of the first light chain and the first heavy chain at a first time;

(c) terminating the expression of the first light chain and the first heavy chain;

(d) causing expression of the second light chain and the second heavy chain after or simultaneously with step (c); and

(e) isolating a four-chain, bispecific antibody that binds to both the first antigen and the second antigen, wherein the four-chain, bispecific antibody comprises the first light and heavy chains and the second light and heavy chains.